

524, 963

(12) INTERNATIONAL PUBLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



Rec'd PCT/PTO 18 FEB 2005



(43) International Publication Date  
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number  
**WO 2004/018044 A2**

(51) International Patent Classification<sup>7</sup>: **A61P 35/00**,  
29/00, A61K 31/497

(21) International Application Number:  
PCT/GB2003/003653

(22) International Filing Date: 20 August 2003 (20.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0219660.8 23 August 2002 (23.08.2002) GB

(71) Applicant (for all designated States except MG, US): **ASTRAZENECA AB** [SE/SE]; S-151 85 Sodertalje (SE).

(71) Applicant (for MG only): **ASTRAZENECA UK LIMITED** [GB/GB]; 15 Stanhope Gate, London, Greater London W1K 1LN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **TONGE, David, William** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). **TAYLOR, Sian, Tomiko** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). **BOYLE, Francis, Thomas** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). **HUGHES, Andrew, Mark** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). **JOHNSTONE, Donna** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park,

Macclesfield, Cheshire SK10 4TG (GB). **ASHFORD, Marianne, Bernice** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). **BARRASS, Nigel, Charles** [GB/GB]; AstraZeneca R & D Alderley, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).

(74) Agent: **ASTRAZENECA**; Global Intellectual Property, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: THERAPEUTIC USE

(57) Abstract: The use of *N*-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide, or a pharmaceutically acceptable salt thereof, in the treatment of cancer and/or pain in a warm blooded animal such as man is described.



WO 2004/018044 A2

(19) World Intellectual Property  
Organization  
International Bureau



Rec'd PCT/PTC 18 FEB 2005



(43) International Publication Date  
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number  
**WO 2004/018044 A3**

(51) International Patent Classification<sup>7</sup>: **A61P 35/00**,  
29/00, A61K 31/497

(GB). BARRASS, Nigel, Charles [GB/GB]; AstraZeneca  
R & D Alderley, Alderley Park, Macclesfield, Cheshire  
SK10 4TG (GB).

(21) International Application Number:  
PCT/GB2003/003653

(74) Agent: **ASTRAZENECA**; Global Intellectual Property,  
Mereside, Alderley Park, Macclesfield, Cheshire SK10  
4TG (GB).

(22) International Filing Date: 20 August 2003 (20.08.2003)

(25) Filing Language: English

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,  
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,  
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(26) Publication Language: English

(30) Priority Data:  
0219660.8 23 August 2002 (23.08.2002) GB

(71) Applicant (*for all designated States except MG, US*): **AS-  
TRAZENECA AB** [SE/SE]; S-151 85 Sodertalje (SE).

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for MG only*): **ASTRAZENECA UK LIM-  
ITED** [GB/GB]; 15 Stanhope Gate, London, Greater Lon-  
don W1K 1LN (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **TONGE, David**,  
**William** [GB/GB]; AstraZeneca R & D Alderley, Alderley  
Park, Macclesfield, Cheshire SK10 4TG (GB). **TAYLOR**,  
**Sian, Tomiko** [GB/GB]; AstraZeneca R & D Alderley,  
Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).  
**BOYLE, Francis, Thomas** [GB/GB]; AstraZeneca R  
& D Alderley, Alderley Park, Macclesfield, Cheshire  
SK10 4TG (GB). **HUGHES, Andrew, Mark** [GB/GB];  
AstraZeneca R & D Alderley, Alderley Park, Maccles-  
field, Cheshire SK10 4TG (GB). **JOHNSTONE, Donna**  
[GB/GB]; AstraZeneca R & D Alderley, Alderley Park,  
Macclesfield, Cheshire SK10 4TG (GB). **ASHFORD**,  
**Marianne, Bernice** [GB/GB]; AstraZeneca R & D Alder-  
ley, Alderley Park, Macclesfield, Cheshire SK10 4TG

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
6 May 2004

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: **N-(3-METHOXY-5-METHYLPYRAZIN-2-YL)-2-(4-[1,3,4-OXADIAZOL-2-YL]PHENYL)PYRIDINE-3  
SULPHONAMIDE AS AN ANTICANCER AGENT**

(57) Abstract: The use of *N*-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide, or a  
pharmaceutically acceptable salt thereof, in the treatment of cancer and/or pain in a warm blooded animal such as man is described.

WO 2004/018044 A3

REVISED VERSION

Rec'd PCT/PTO

18 FEB 2005

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number  
**WO 2004/018044 A3**

(51) International Patent Classification?: **A61P 35/00**,  
29/00, A61K 31/497

R & D Alderley, Alderley Park, Macclesfield, Cheshire  
SK10 4TG (GB).

(21) International Application Number:  
PCT/GB2003/003653

(74) Agent: **ASTRAZENECA**; Global Intellectual Property,  
Mereside, Alderley Park, Macclesfield, Cheshire SK10  
4TG (GB).

(22) International Filing Date: 20 August 2003 (20.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0219660.8 23 August 2002 (23.08.2002) GB

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,  
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,  
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(71) Applicant (*for all designated States except MG, US*): **AS-  
TRAZENECA AB** [SE/SE]; S-151 85 Sodertalje (SE).

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for MG only*): **ASTRAZENECA UK LIM-  
ITED** [GB/GB]; 15 Stanhope Gate, London, Greater Lon-  
don W1K 1LN (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **TONGE, David**,  
William [GB/GB]; AstraZeneca R & D Alderley, Alderley  
Park, Macclesfield, Cheshire SK10 4TG (GB). **TAYLOR**,  
Sian, Tomiko [GB/GB]; AstraZeneca R & D Alderley,  
Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).  
**BOYLE, Francis, Thomas** [GB/GB]; AstraZeneca R  
& D Alderley, Alderley Park, Macclesfield, Cheshire  
SK10 4TG (GB). **HUGHES, Andrew, Mark** [GB/GB];  
AstraZeneca R & D Alderley, Alderley Park, Maccles-  
field, Cheshire SK10 4TG (GB). **JOHNSTONE, Donna**  
[GB/GB]; AstraZeneca R & D Alderley, Alderley Park,  
Macclesfield, Cheshire SK10 4TG (GB). **ASHFORD**,  
Marianne, Bernice [GB/GB]; AstraZeneca R & D Alder-  
ley, Alderley Park, Macclesfield, Cheshire SK10 4TG  
(GB). **BARRASS, Nigel, Charles** [GB/GB]; AstraZeneca

Published:

— with international search report

(88) Date of publication of the international search report:  
6 May 2004

Date of publication of the revised international search  
report: 24 June 2004

(15) Information about Correction:

see PCT Gazette No. 26/2004 of 24 June 2004, Section II

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: **N-(3-METHOXY-5-METHYLPYRAZIN-2-YL)-2-(4-[1,3,4-OXADIAZOL-2-YL]PHENYL)PYRIDINE-3  
SULPHONAMIDE AS AN ANTICANCER AGENT**

(57) Abstract: The use of *N*-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide, or a  
pharmaceutically acceptable salt thereof, in the treatment of cancer and/or pain in a warm blooded animal such as man is described.

WO 2004/018044 A3

## INTERNATIONAL SEARCH REPORT

Intern Application No

PCT/GB 03/03653

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 A61P35/00 A61P29/00 A61K31/497

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/40681 A (ZENECA LTD) 19 December 1996 (1996-12-19) cited in the application page 2, line 6 page 21, lines 28-30 claim 11	1-25
Y	WO 01/44239 A (BRISTOL MYERS SQUIBB CO ;MURUGESAN NATESAN (US); GU ZHENGXIANG (US) 21 June 2001 (2001-06-21) page 48, paragraph 1 ----- -/--	1-22

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

26 February 2004

Date of mailing of the international search report

12 03. 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Skjöldebrand, C

## INTERNATIONAL SEARCH REPORT

Intern

Application No

PCT/GB 03/03653

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CARDUCCI M A ET AL: "ENDOTHELIN RECEPTOR ANTAGONIST, ABT-627, FOR PROSTATE CANCER: INITIAL TRIAL RESULTS" JOURNAL OF UROLOGY, BALTIMORE, MD, US, vol. 161, no. 4, SUPPL, April 1999 (1999-04), page 176, XP001037609 ISSN: 0022-5347 abstract	1-22
Y	NELSON J B ET AL: "THE ROLE OF ENDOTHELIN-1 AND ENDOTHELIN RECEPTOR ANTAGONISTS IN PROSTATE CANCER" BJU INTERNATIONAL, BLACKWELL SCIENCE, OXFORD, GB, vol. 85, no. SUPPL 2, April 2000 (2000-04), pages 45-48, XP008007943 ISSN: 1464-4096 the whole document	1-22
Y	JARVIS M F ET AL: "ABT-627, AN ENDOTHELIN ETA RECEPTOR-SELECTIVE ANTAGONIST, ATTENUATES TACTILE ALLODYNIA IN A DIABETIC RAT MODEL OF NEUROPATHIC PAIN" EUROPEAN JOURNAL OF PHARMACOLOGY, AMSTERDAM, NL, vol. 388, no. 1, 24 January 2000 (2000-01-24), pages 29-35, XP001152675 ISSN: 0014-2999 abstract	23-25
Y	WO 02/49630 A (SQUIBB BRISTOL MYERS CO ; LEBWOHL DAVID E (US)) 27 June 2002 (2002-06-27) claims	23-25
Y	DATABASE WPI Section Ch, Week 200163 Derwent Publications Ltd., London, GB; Class B03, AN 2001-565331 XP002271565 & WO 01/60370 A (YAMANOUCHI PHARM CO LTD) 23 August 2001 (2001-08-23) abstract	23-25

# INTERNATIONAL SEARCH REPORT

In International application No.  
T/GB 03/03653

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-22

The use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-  
'1,3,4-oxadiazol-2-yl!phenyl)pyridine-3 sulphonamide in the  
manufacture of a medicament for use in the treatment of  
cancer in a warm-blooded animal.

---

2. claims: 23-25

The use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-  
'1,3,4-oxadiazol-2-yl!phenyl)pyridine-3 sulphonamide in the  
manufacture of a medicament for use in the prevention and  
treatment of pain in a warm-blooded animal.

---

## INTERNATIONAL SEARCH REPORT

International Application No.

P GB 03/03653

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9640681	A	19-12-1996	AT 209200 T	15-12-2001
			AU 715041 B2	13-01-2000
			AU 5840396 A	30-12-1996
			BR 9608611 A	11-05-1999
			CA 2219742 A1	19-12-1996
			CN 1192739 A ,B	09-09-1998
			CZ 9703887 A3	18-03-1998
			DE 69617236 D1	03-01-2002
			DE 69617236 T2	11-07-2002
			DK 832082 T3	21-05-2002
			EP 0832082 A1	01-04-1998
			ES 2168487 T3	16-06-2002
			WO 9640681 A1	19-12-1996
			HK 1005801 A1	20-12-2002
			HR 960272 A1	31-08-1997
			HU 9802300 A2	28-10-1999
			IL 122464 A	23-05-2002
			JP 11509175 T	17-08-1999
			JP 3193058 B2	30-07-2001
			NO 975700 A	05-12-1997
			NZ 308619 A	28-01-2000
			PL 324660 A1	08-06-1998
			PT 832082 T	29-04-2002
			SI 832082 T1	30-04-2002
			SK 168097 A3	06-05-1998
			TR 9701502 T1	21-03-1998
			US 6060475 A	09-05-2000
			US 6258817 B1	10-07-2001
			US 5866568 A	02-02-1999
			ZA 9604615 A	09-12-1996
WO 0144239	A	21-06-2001	AU 2092601 A	25-06-2001
			CA 2395088 A1	21-06-2001
			EP 1237888 A2	11-09-2002
			JP 2003520785 T	08-07-2003
			WO 0144239 A2	21-06-2001
			US 2002143024 A1	03-10-2002
WO 0249630	A	27-06-2002	AU 4173602 A	01-07-2002
			WO 0249630 A2	27-06-2002
			US 2002082285 A1	27-06-2002
WO 0160370	A	23-08-2001	AU 7961400 A	27-08-2001
			BR 0017120 A	14-01-2003
			CA 2395711 A1	18-07-2002
			CN 1434715 T	06-08-2003
			EP 1256344 A1	13-11-2002
			HU 0204139 A2	28-05-2003
			WO 0160370 A1	23-08-2001
			JP 2001302514 A	31-10-2001